Carbonyl “Self” Rxns

A/K Rxns (“Aldol”)

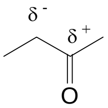
Ester Rxns (“Claisen”)

Michael & Robibnson Rxns

Ref	17: 4 – 7; 9b ; 19: 1, 2, 9
Prob	17: 7 – 9, 12, 13, 18, 19, 21, 26
	19: 1- 2
Adv Rdg	20: 1 – 6; 25: 4

General

- carbonyl C , electrophilic
- α C, nucleophilic



∴ 2 molecules can “self – react”

Ex.

- applies to A/K’s

Mech.:

aldol = β-hydroxy carbonyl cmpd

Comment: happens also under acidic conditions

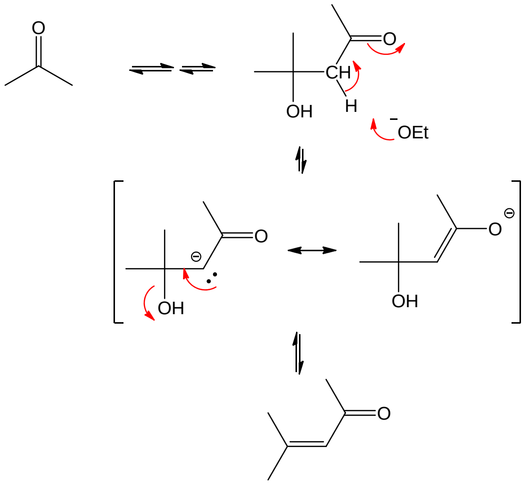
(you can self-derive; I will skip)

Dehydration = Condensation

(“enone form^{n}”)

aldol formation (C – C bond form^{n}) is often followed by loss of H_2O

Ex



α,β - unsaturated carbonyl cmpd = "enone"

Notes:

Generally

1.) aldehydes:

equilibrium aldol dimer ⟺ aldehyde monomer

is in favor of dimer; aldol can be isolated;

can be driven to enone by extra heat, time ...

2.) ketones

equilibrium in favor of monomer;

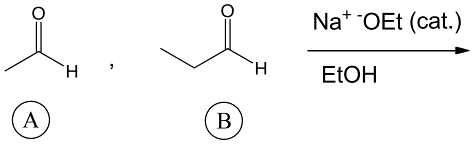
must be driven to enone to make product

3.) "reverse aldol" (dimer → monomer)

may be possible given appropriate experimental conditions

Mixed ("Crossed") Aldol

- between 2 different A/K cmpds;
- usually gives mixtures



mixtures of aldols; "USELESS"

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mixed ...

- can be successful, if

1.) B can form enolate ("enolizable");

A cannot (normally, has no α H), but has reactive carbonyl C

Ex.

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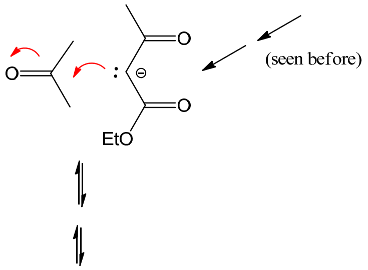
mixed ...

2.) B is doubly activated (malonic ester, etc. ...);

A is normal ("mono carbonyl")

Ex.



(seen before)

mixed ...

3.) use LDA methodology

- i.) produce enolate of one A/K with LDA at –78°C (fast, quantitatively, irreversibly)
- ii.) mix w/ 2nd A/K and allow to warm to r.t.
- iii.) work up w/ H_3O^+

Ex.

Intramolecular Aldol

can occur when 2 A/K carbonyls are present in one molecule; esp.

A.) 1,4 dicarbonyl → cyclopentane derivative

b.) 1,5 dicarbonyl → cyclohexane derivative

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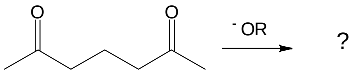
intramolecular ...

Ex.

N.B.:

rxn essentially “one-way” due to cyclization

HMWK: 

Claisen Rxn

- between 2 ester molecules
- w/ 1 equiv. of base
- “enolate” reacts with “keto”, in typical “nucleophilic acyl substitution” fashion, going through “tetrahedral intermediate”

Ex., overall rxn

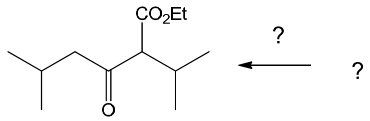
Claisen ...

Mech.

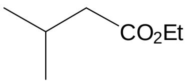
N.B.:
final step irreversible;
consumes 1 equiv. of base;
drives rxn "one-way";
need to acidic work-up to get product: β-ketoester

Claisen ....

Practice as HMWK; incl. mechanism



Ans.

use  as starting material and

repeat the mechanism from the previous page

Dieckman Rxn

(≡ *Intramolecular Claisen*)

esp.: 1,6 & 1,7 diesters give ring systems;
↓ ↓
5C-ring 6C-ring

HMWK: cyclyze 1,7 diester; w/ mech.

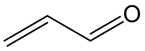
HMWK Answer

Michael Addition

General Background

Terminology

“α,β unsaturated carbonyl” = “conjugated carbonyl” = “enone”



(somewhat reminiscent of 1,3 dienes;

but in the 1st step of 1,3- dienes electrophiles are added;

while enones are attacked by nucleophiles)

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general ...

resonance structures of enones

Nu: can attack at pos^n 2) or pos^n 4); giving

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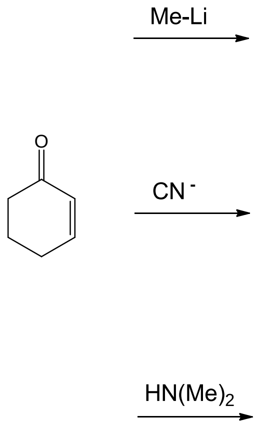
general ...

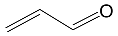
- attack at pos^n 2) requires less activation energy (E_a) = kinetic product
- attack at pos^n 4) require more E_a, but product is more stable (carbonyl group is regenerated = thermodynamic product
- aggressive, strong Nu’s (e.g., $LiAlH_4$, R-Li form 1,2 product irreversibly: *kinetic product*
- mild, weak nucleophiles (amines, CN^-, **enolates)** can also form 1,2 adduct, but can equilibrate to the 1,4 adduct: *thermodynamic product* giving mostly 1,4 adduct, if allowing sufficient time.

Practice

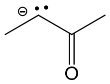


Michael Add^n w/ Enolates

Michael Acceptor



Michael Donor



conj. carbonyl:
A/K, ester, ...

mono or 1,3 di
carbonyl cmpds

rxn conditions: 1.) NaOH(cat.)/THF/H_2O, or
2.) NaOEt(cat.)/EtOH

Simple Ex.

Robinson Rxn

= combination of Michael & internal aldol rxn; need increase in temp.

Ex. cont^d:

Note: other aldols could form,
but all these rxns are equil. rxns;
and the cyclohexenone is the most stable !!

Practice: Retrosynthetic Analysis